

What is claimed is:

1. A computer implemented method for selecting oligonucleotide probes

comprising:

a) predicting hybridization intensities of a plurality of candidate probes;

5 b) predicting quantitative responses of said candidate probes to the amount of their targets; and

c) selecting said probes from said candidate probes according to said hybridization intensities and said quantitative response.

10 2. The method of Claim 1 wherein said quantitative response is the slope of the response curve of said probe.

3. The method of Claim 2 wherein said hybridization intensity (I) is determined using the equation:

$$Ln(I) = \sum_{i=1}^{3N} W_i S_i + C_2$$

Or

$$Ln(I) = \sum_{i=1}^{3N} W_i S_i$$

wherein said W_i is a weight coefficient; S_i is a functional of said sequence of said probe; N is the number of bases of said probe; and C_2 is a constant.

4. The method of Claim 3 wherein said weight coefficient is determined using multiple linear regression analysis.

5. The method of Claim 4 further comprising predicting mismatch hybridization

5 intensities of corresponding mismatch probes of said candidate probes and wherein said selecting step is also based upon said mismatch hybridization intensities.

6. The method of Claim 5 wherein said mismatch probes are different from their corresponding candidate probes in one base pair in the middle of their sequences.

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7. The method of Claim 6 wherein said mismatch hybridization intensities are predicted according to the sequences of said candidate genes.

8. The method of Claim 3 further comprising filtering out a subset of said candidate
15 probes, wherein said subset probes have apparent affinity constant above a threshold.

9. The method of claim 8 wherein the threshold is above 5 for \ln (apparent affinity constant).

20 10. The method of claim 9 wherein the threshold is above 6.

11. The method of claim 10 wherein the threshold is above 7.

12. The method of Claim 7 wherein mismatch hybridization intensities are determined according to the following equation:

$$Ln(I) = \sum_{i=1}^{3N} W_i' S_i + C_2' \quad \text{or}$$

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$$Ln(I) = \sum_{i=1}^{3N} W_i' S_i$$

wherein said W_i' is a weight coefficient; S_i is a functional of said sequence of said probe; N is the number of bases of said probe; and C_2' is a constant.

13. The method of Claim 12 wherein said selecting step comprises calculating a unified quality score based upon predicted hybridization intensities.

14. A computer software product for selecting oligonucleotide probes comprising:
computer program code for predicting hybridization intensities of a plurality of candidate probes;

computer program code for predicting quantitative responses of said candidate probes to the amount of their targets;

computer program code for selecting said probes from said candidate probes according to said hybridization intensities and said quantitative response; and
a computer readable media for storing said computer program codes.

15. The computer software product of Claim 14 wherein said quantitative response is the slope of the response curve of said probe.

16. The computer software product of Claim 15 wherein said hybridization intensity

5 (I) is determined using the equation:

$$\ln(I) = \sum_{i=1}^{3N} W_i S_i + C_2$$

Or

$$\ln(I) = \sum_{i=1}^{3N} W_i S_i$$

wherein said W_i is a weight coefficient; S_i is a functional of said sequence of said probe; N is the number of bases of said probe; and C_2 is a constant.

10 17. The computer software product of Claim 16 wherein said weight coefficient is determined using multiple linear regression analysis.

15 18. The computer software product of Claim 17 further comprising computer program code for predicting mismatch hybridization intensities of corresponding mismatch probes of said candidate probes and wherein said selecting step is also based upon said mismatch hybridization intensities.

19. The computer software product of Claim 18 wherein said mismatch probes are different from their corresponding candidate probes in one base pair in the middle of their sequences.

5 20. The computer software product of Claim 19 wherein said mismatch hybridization intensities are predicted according to the sequences of said candidate genes.

21. The computer software product of Claim 20 wherein mismatch hybridization intensities are determined according to the following equation:

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$$Ln(I) = \sum_{i=1}^{3N} W'_i S_i + C'_2 \quad \text{or}$$

$$Ln(I) = \sum_{i=1}^{3N} W'_i S_i$$

wherein said W'_i is a weight coefficient; S_i is a functional of said sequence of said probe; N is the number of bases of said probe; and C'_2 is a constant.

15 22. The computer software product of Claim 14 further comprising computer program code of filtering out a subset of said candidate probes, wherein said subset probes have apparent affinity constant above a threshold.

20 23. The computer software product of claim 22 wherein the threshold is above 5 for ln (apparent affinity constant).

24. The computer software product of claim 23 wherein the threshold is above 6.

25. The computer software product of claim 24 wherein the threshold is above 7.

26. The computer software of Claim 21 wherein said computer program code for selecting comprises computer program code for calculating a unified quality score based upon predicted hybridization intensities.

27. A system for selecting nucleic acid probes, comprising:

a processor; and

a memory being coupled to the processor, the memory storing a plurality machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, said logical steps including:

e) predicting hybridization intensities of a plurality of candidate probes;

f) predicting quantitative responses of said candidate probes to the amount of their targets; and

g) selecting said probes from said candidate probes according to said hybridization intensities and said quantitative response.

28. The system of Claim 27 wherein said quantitative response is the slope of the response curve of said probe.

29. The system of Claim 28 wherein said hybridization intensity (I) is determined using the equation:

$$Ln(I) = \sum_{i=1}^{3N} W_i S_i + C_2$$

Or

$$Ln(I) = \sum_{i=1}^{3N} W_i S_i$$

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wherein said W_i is a weight coefficient; S_i is a functional of said sequence of said probe; N is the number of bases of said probe; and C_2 is a constant.

30. The system of Claim 29 wherein said weight coefficient is determined using multiple linear regression analysis.

31. The system of Claim 27 wherein said logic steps further comprises predicting mismatch hybridization intensities of corresponding mismatch probes of said candidate probes and wherein said selecting step is also based upon said mismatch hybridization intensities.

32. The system of Claim 31 wherein said mismatch probes are different from their corresponding candidate probes in one base pair in the middle of their sequences.

33. The system of Claim 32 wherein said mismatch hybridization intensities are predicted according to the sequences of said candidate genes.

34. The system of Claim 33 wherein mismatch hybridization intensities are

5 determined according to the following equation:

$$Ln(I) = \sum_{i=1}^{3N} W'_i S_i + C_2' \quad \text{or}$$

$$Ln(I) = \sum_{i=1}^{3N} W'_i S_i$$

wherein said W'_i is a weight coefficient; S_i is a functional of said sequence of said probe; N is the number of bases of said probe; and C_2' is a constant.

10 35. The system of Claim 27 wherein said logic steps further comprises filtering out a subset of said candidate probes, wherein said subset probes have apparent affinity constant above a threshold.

15 36. The system of claim 35 wherein the threshold is above 5 for ln (apparent affinity constant).

37. The system of claim 35 wherein the threshold is above 6.

20 38. The system of claim 35 wherein the threshold is above 7.

39. The system of Claim 34 wherein said selecting step comprises calculating a unified quality score based upon predicted hybridization intensities.

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